skNAC, a Smyd1-interacting transcription factor, is involved in cardiac development and skeletal muscle growth and regeneration.

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Public Summary:
Cardiac and skeletal muscle development and maintenance require complex interactions between DNA-binding proteins and chromatin remodeling factors. We previously reported that Smyd1, a muscle-restricted histone methyltransferase, is essential for cardiogenesis and functions with a network of cardiac regulatory proteins. Here we show that the muscle-specific transcription factor skNAC is the major binding partner for Smyd1 in the developing heart. Targeted deletion of skNAC in mice resulted in partial embryonic lethality by embryonic day 12.5, with ventricular hypoplasia and decreased cardiomyocyte proliferation that were similar but less severe than in Smyd1 mutants. Expression of Irx4, a ventricle-specific transcription factor down-regulated in hearts lacking Smyd1, also depended on the presence of skNAC. Viable skNAC(-/-) adult mice had reduced postnatal skeletal muscle growth and impaired regenerative capacity after cardiotoxin-induced injury. Satellite cells isolated from skNAC(-/-) mice had impaired survival compared with wild-type littermate satellite cells. Our results indicate that skNAC plays a critical role in ventricular cardiomyocyte expansion and regulates postnatal skeletal muscle growth and regeneration in mice.

Scientific Abstract:
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